VASCULAR PROSTHESIS WITH ANASTOMOTIC MEMBER

FIELD AND BACKGROUND OF THE INVENTION

The present invention relates to implantable devices, and, more particularly, to a vascular prosthesis with anastomotic device.

Diseases affecting the vascular system are either congenital or acquired. An acquired vascular disease can result from living habits, infections or injuries during embryonic life, or at any time following birth. Some diseases primarily affect the blood vessels; others only the heart itself.

Atherosclerosis is the major disease that affects the blood vessels. This disease may have its beginnings early in life and is first noted as a thickening of the arterial walls. This thickening is an accumulation of fat, fibrin, cellular debris and calcium. The resultant narrowing of the internal lumen of the vessel is called stenosis. Vessel stenosis impedes and reduces blood flow. Hypertension and dysfunction of the organ or area of the body that suffered the impaired blood flow can result. As the buildup on the inner wall of a vessel thickens, the vessel wall loses the ability to expand and contract. Additionally, the vessel loses its viability and becomes weakened and susceptible to bulging, also known as aneurysm. In the presence of hypertension or elevated blood pressure, aneurysms frequently dissect and ultimately rupture.

Small vessels, such as the arteries that supply blood to the heart, legs, intestines and other areas of the body, are particularly susceptible to atherosclerotic narrowing. The loss of blood supply to the leg or segment of the intestine may result in gangrene. Atherosclerotic narrowing of the coronary arteries impedes limits and in some instances prevents blood flow to regional areas of the heart. Depending upon its severity and location within the coronary circulation, pain, cardiac dysfunction or death may result.

Vascular complications produced by atherosclerosis, such as, stenosis, aneurysm, rupture and occlusion are, in the majority of cases, managed either medically or surgically. Control and elimination of hypertension is the more effective form of medical management. Typically, surgical intervention is instituted in cases in which the atherosclerotic disease is advanced and the attendant complications jeopardize the health of the patient.

Aneurysms and stenosis of major arteries are best corrected by a plastic reconstruction that does not require any synthetic graft or patch materials. However, if the disease is extensive and the vessel is no longer reliable, the common practice is to replace the vessel or a portion thereof by a graft. In such cases, the involved vessel section is transected and removed and an artificial blood vessels is sewn into place. Another common practice for treating extensive stenosis, as well as other coronary heart diseases, is stent deployment. A stent is a generally cylindrical prosthesis introduced via a catheter into a lumen of a body vessel in a configuration having a generally reduced diameter and then expanded to the diameter of the vessel. The stent may be self-expanding, or it may be expandable by means of an inflatable portion of the catheter, such as a balloon. In its expanded configuration, the stent supports and reinforces the vessel walls while maintaining the vessel in an open, unobstructed condition.

Artificial blood vessels, vascular prostheses and stents, including self-expanding, inflation assisted expandable and inflation expandable stents, are well known and widely available in a variety of designs and configurations. Inflation expandable and inflation assisted expandable stents are expanded via outward radial pressure such as that provided by a balloon disposed underneath the stent during inflation of the balloon.

Of particular interest are prosthetic devices made of, or coated with, polymer materials which typically exhibit a microporous structure that in general allows healthy tissue growth and cell endothelization, thus contributing to the long term healing of the prostheses. Prostheses having sufficient porous structure tend to promote tissue ingrowth and cell endothelization along their inner surface.

Stents with fiber polymer coating promote preparation of porous coatings with better grafting and highly developed surface. For example, U.S. Patent No. 5,549,663 discloses a stent graft having a coating made of polyurethane fibers which are applied using conventional wet spinning techniques. Prior to the covering process, a medication is introduced into the polymer.

A more promising method for stent coating is electrospinning. Electrospinning is a method for the manufacture of ultra-thin synthetic fibers which reduces the number of technological operations required in the manufacturing process and improves the product being manufactured in more than one way.

The process of electrospinning creates a fine stream or jet of liquid that upon proper evaporation of a solvent or liquid to solid transition state yields a nonwoven structure. The fine stream of liquid is produced by pulling a small amount of polymer solution through space by using electrical forces. More particularly, the electrospinning process involves the subjection of a liquefied substance, such as polymer, into an electric field, whereby the liquid is caused to produce fibers that are drawn by electric forces to an electrode, and are, in addition, subjected to a hardening procedure. In the case of liquid which is normally solid at room temperature, the hardening procedure may be mere cooling; however other procedures such as chemical hardening (polymerization) or evaporation of solvent may also be employed. The produced fibers are collected on a suitably located precipitation device and subsequently stripped from it. The sedimentation device is typically shaped in accordance with the desired geometry of the final product, which may be for example tubular, flat or even an arbitrarily shaped product.

The use of electrospinning for stent coating permits to obtain durable coating with wide range of fiber thickness (from tens of nanometers to tens of micrometers), achieves exceptional homogeneity, smoothness and desired porosity distribution along the coating thickness. Stents themselves do not encourage normal cellular invasion and therefore can lead to an undisciplined development of cells in the metal mesh of the stent, giving rise to cellular hyperplasia. When a stent is electrospinningly coated by a graft of a porous structure, the pores of the graft component are invaded by cellular tissues from the region of the artery surrounding the stent. Moreover, diversified polymers with various biochemical and physico-mechanical properties can be used in stent coating. Examples of electrospinning methods in stent manufacturing are found in U.S. Patent Nos. 5,639,278, 5,723,004, 5,948,018, 5,632,772 and 5,855,598.

As the stent expands within the blood vessel, it then cracks the plaques on the wall of the artery and produces shards or fragments whose sharp edges cut into the tissue. This causes internal bleeding and a possible local infection, which if not adequately treated, may spread and adversely affect other parts of the body. Additionally, excessive natural healing process in response to arterial injuries, oftentimes results in re-closure (termed restenosis) of the treated artery. The natural healing process may continue until a complete reclusion of the artery.

The risk of vessel damage during stent implantation may be lowered through the use of a soft stent serving to improve the biological interface between the stent and the artery and thereby reduce the risk that the stent will inflict damage during implantation. Examples of polymeric stents or stent coatings with biocompatible fibers are found in, for example, U.S. Patent Nos. 6,001,125, 5,376,117 and 5,628,788, all of which are hereby incorporated by reference.

U.S. Patent No. 5,948,018 discloses a graft composed of an expansible stent component covered by an elastomeric polymeric graft component which, because of its stretchability, does not inhibit expansion of the stent. The graft component is fabricated by electrospinning to achieve porosity hence to facilitate normal cellular growth.

The U.S. Patent No. 5,628,788 describes endoluminal self-expanding stent-graft with elastic jacket made of textile polyethylene terephthalate mesh. Such graft is able to repeat the stent shape and sizes after its expansion, thus providing easy connection with the operated vessel, on the one hand, and graft support within the entire life period, on the other hand. To achieve required sealing and prevent blood leakage, the stent-graft is supplemented by a porous elastomeric liner affixed to the mesh with an elastomeric adhesive. The liner increases the stent-graft as-folded diameter. Similar solutions were used in U.S. Patents Nos. 5,632,772, 5,723,004, 5,855,598 and 5,948,018.

Even though coronary artery bypass surgery and other blood vessel implantation procedures are widely practiced and have become a routine procedure in hospitals throughout the world, they are not without certain operative limitations that would best be avoided. The procedure of stapling the graft to the host vessel, commonly termed anastomosis, is typically performed by suturing which may result in less than optimal result. Moreover, prior art vascular grafts are inapplicable for the treatment of, for example, complicated aneurysms such as abdominal, common iliac, external iliac, rental or mesenteric arteries, in which four or five arteries must be supported simultaneously.

There is thus a widely recognized need for, and it would be highly advantageous to have a vascular prosthesis with anastomotic device, devoid of the above limitations.

SUMMARY OF THE INVENTION

According to one aspect of the present invention there is provided a medical device for implantation in a vessel, comprising at least one anastomotic member at least partially interposing a non-woven liner of electrospun fibers and a non-woven cover of electrospun fibers; the at least one anastomotic member being designed for engaging at least one end of the medical device to a wall of the vessel upon implantation of the medical device within the vessel.

According to another aspect of the present invention there is provided a kit for performing an end-to-side anastomosis procedure, comprising: a medical device for implantation in a vessel as described herein; and a accessory device for forming an opening in the wall of the vessel, the accessory device comprising a tubular encapsulation designed and constructed for receiving the medical device, a cutting member integrated with or attached to an end of the tubular encapsulation and capable of forming an opening in the wall of the vessel, and a vacuum channel for channeling efflux of biological material from the tubular encapsulation.

According to further features in preferred embodiments of the invention described below, the medical device forms a furcating structure having a plurality of tubular branches.

According to still further features in the described preferred embodiments the non-woven liner and the non-woven cover form a tubular structure.

According to still further features in the described preferred embodiments the at least one anastomotic member is adapted for end-to-end anastomosis.

According to still further features in the described preferred embodiments at least one end of the furcating structure is adapted for end-to-end anastomosis.

According to still further features in the described preferred embodiments at least one end of the tubular structure is adapted for end-to-end anastomosis.

According to still further features in the described preferred embodiments at least one anastomotic member is adapted for end-to-side anastomosis.

According to still further features in the described preferred embodiments at least one end of the furcating structure is adapted for end-to-side anastomosis.

According to still further features in the described preferred embodiments at least one end of the tubular structure is adapted for end-to-side anastomosis.

According to still further features in the described preferred embodiments the at least one anastomotic member protrudes out of the non-woven cover.

According to still further features in the described preferred embodiments the at least one anastomotic member comprises a single anastomotic member extending over the tubular structure and protruding from at least one end of the tubular structure.

According to still further features in the described preferred embodiments the at least one anastomotic member comprises a first anastomotic member engaging a first end of the tubular structure, and a second anastomotic member engaging a second end of the tubular structure.

According to still further features in the described preferred embodiments the at least one anastomotic member is flush with the non-woven cover.

According to still further features in the described preferred embodiments the at least one anastomotic member comprises an expandable supporting element. According to still further features in the described preferred embodiments the engagement of the at least one end of the medical device to the wall of the vessel is effected by pressure generated by an expansion of the expandable supporting element.

According to still further features in the described preferred embodiments the medical device further comprises a ring-shaped protuberance designed and constructed to prevent the device from falling into a lumen of the vessel.

According to still further features in the described preferred embodiments the at least one anastomotic member comprises a plurality of hooks for connecting the device to the wall of the vessel.

According to still further features in the described preferred embodiments the plurality of hooks is designed and constructed such that when the expandable supporting element expands, the plurality of hooks pierce the wall of the vessel, thereby mounting the device to the vessel.

According to still further features in the described preferred embodiments the plurality of hooks is designed and constructed to pierce an inner wall of the vessel and to protrude out of an outer wall of the vessel.

According to still further features in the described preferred embodiments the medical device further comprises at least one perforated member mounted on the non-woven cover in a manner such that protruding portions of the plurality of hooks engage the at least one perforated member.

According to still further features in the described preferred embodiments the medical device further comprises a pressing ring for bending protruding portions of the plurality of hooks, thereby perverting detachment of the plurality of hooks from the wall of the vessel.

According to still further features in the described preferred embodiments the medical device further comprises a thrust ring for thrusting the pressing ring.

According to still further features in the described preferred embodiments the medical device further comprises a lever for establishing contact between the thrust ring and the pressing ring.

According to still further features in the described preferred embodiments the medical device further comprises at least one adhesive layer for adhering at least two of: the non-woven liner, the non-woven cover and the at least one anastomotic member.

According to still further features in the described preferred embodiments the at least one adhesive layer is formed of a thermoplastic polymer having a characteristic melting temperature which is lower than characteristic melting temperatures of the electrospun fibers of each of the non-woven liner and the non-woven cover.

According to still further features in the described preferred embodiments the at least one adhesive layer comprises silicon.

According to still further features in the described preferred embodiments the electrospun fibers are made of a biocompatible polymer. According to still further features in the described preferred embodiments the electrospun fibers are manufactured from a liquefied polymer. According to still further features in the described preferred embodiments the electrospun fibers of the non-woven liner comprise polyethylene fibers and polyester fibers. According to still further features in the described preferred embodiments the electrospun fibers of the non-woven cover comprise polyethylene fibers and polyester fibers.

According to yet another aspect of the present invention there is provided a method of manufacturing a medical device for implantation in a vessel, the method comprising: providing at least one anastomotic member designed for engaging a wall of the vessel; electrospinning a first liquefied polymer on a precipitation electrode, thereby providing a non-woven liner of electrospun fibers; mounting the at least one anastomotic member onto the precipitation electrode; and electrospinning a second

liquefied polymer on at least one of: the precipitation electrode, the non-woven liner and the at least one anastomotic member, so as to provide a non-woven cover of electrospun fibers.

According to further features in preferred embodiments of the invention described below, the electrospinning of the second liquefied polymer is done such that the at least one anastomotic member protrudes out of the non-woven cover.

According to still further features in the described preferred embodiments the electrospinning of the second liquefied polymer is done such that the at least one anastomotic member is flush with the non-woven cover.

According to still further features in the described preferred embodiments the method further comprises mounting at least one perforated member onto the non-woven cover, wherein the at least one perforated member is designed and constructed to receive protruding portions of the plurality of hooks.

According to still further features in the described preferred embodiments the method further comprises mounting a pressing ring on the non-woven cover, wherein the pressing ring is designed and constructed for bending protruding portions of the plurality of hooks. According to still further features in the described preferred embodiments the device further comprises mounting a thrust ring onto the non-woven cover, wherein the thrust ring is designed and constructed for thrusting the pressing ring. According to still further features in the described preferred embodiments the device further comprises connecting a lever to the thrust ring and the pressing ring.

According to still further features in the described preferred embodiments the method further comprises repeating the electrospinning of the first and the second liquefied polymers for different orientations of the precipitation electrode, so as to form a furcating structure having a plurality of tubular branches.

According to still further features in the described preferred embodiments the method further comprises applying pressure on at least one of the non-woven liner, the non-woven cover and the at least one anastomotic member.

According to still further features in the described preferred embodiments the method further comprises electrospinning a third liquefied polymer prior to the mounting of the anastomotic member, wherein a boiling point of the third liquefied polymer is higher than a boiling point of the first liquefied polymer.

According to still further features in the described preferred embodiments the method further comprises electrospinning a fourth liquefied polymer prior to the electrospinning of the second liquefied polymer, wherein a boiling point of the fourth liquefied polymer is higher than a boiling point of the second liquefied polymer.

According to still further features in the described preferred embodiments the method further comprises applying at least one adhesive layer on at least one of the non-woven liner and the at least one anastomotic member.

According to still further features in the described preferred embodiments the application of the at least one adhesive layer is effected by electrospinning.

According to still further features in the described preferred embodiments the at least one adhesive layer is formed of a thermoplastic polymer having a characteristic melting temperature which is lower than characteristic melting temperatures of the first and the second liquefied polymers.

According to still further features in the described preferred embodiments the method further comprises heating the device to a temperature which is above the characteristic melting temperature of the thermoplastic polymer and below the characteristic melting temperatures of the first and the second liquefied polymers.

According to still further features in the described preferred embodiments the applying the at least one adhesive layer comprises dipping the at least one anastomotic member in an adhesive solution prior to the mounting of the at least one anastomotic member. According to still further features in the described preferred embodiments the method further comprises heating the adhesive solution. According to still further features in the described preferred embodiments the adhesive solution comprises silicon.

According to still further features in the described preferred embodiments the method further comprises electrospinning an additional liquefied polymer on at least one of: the precipitation electrode, the non-woven liner, the at least one anastomotic member and the non-woven liner.

According to still further features in the described preferred embodiments at least one of the first liquefied polymer and the second liquefied polymer comprises a polyurethane.

According to still further features in the described preferred embodiments the additional liquefied polymer comprises a polyester.

According to still further features in the described preferred embodiments the additional liquefied polymer comprises a mixture of a polyester and a polyurethane.

According to still further features in the described preferred embodiments the electrospinning of the additional liquefied polymer and the electrospinning of the first liquefied polymer is substantially contemporaneously.

According to still further features in the described preferred embodiments the electrospinning of the additional liquefied polymer and the electrospinning of the second liquefied polymer is substantially contemporaneously.

According to still further features in the described preferred embodiments the electrospinning of the additional liquefied polymer and the electrospinning of the first liquefied polymer is performed alternatingly.

According to still further features in the described preferred embodiments the electrospinning of the additional liquefied polymer and the electrospinning of the second liquefied polymer is performed alternatingly.

According to still further features in the described preferred embodiments the electrospun fibers of the non-woven liner and/or the non-woven cover are aligned at a predetermined orientation relative to a longitudinal axis of the device.

According to still further features in the described preferred embodiments the electrospun fibers of the non-woven liner and/or the non-woven cover are randomly aligned.

According to still further features in the described preferred embodiments at least a portion of the electrospun fibers of the non-woven liner and/or the non-woven cover are aligned substantially along a circumferential direction of the non-woven liner and/or the non-woven cover.

According to still further features in the described preferred embodiments at least one of the non-woven liner and the non-woven cover comprises at least one medicament incorporated therein, for delivery of the at least one medicament into a body vasculature during or after implantation of the device within the body vasculature.

According to still further features in the described preferred embodiments the expandable supporting element is designed and constructed for dilating a constricted blood vessel in a body vasculature.

According to still further features in the described preferred embodiments the non-woven liner and the non-woven cover are each independently characterized by a porosity of at least 50 %.

According to still further features in the described preferred embodiments the non-woven liner and the non-woven cover are each independently characterized by a porosity of from about 50 % to about 85 %.

According to still further features in the described preferred embodiments a thickness of the electrospun fibers is from about 100 nanometers to about 500 nanometers.

According to still further features in the described preferred embodiments at least a portion of the electrospun fibers is made of a biodegradable polymer.

According to still further features in the described preferred embodiments at least a portion of the electrospun fibers is made of a biostable polymer.

According to still further features in the described preferred embodiments at least a portion of the electrospun fibers is made of a combination of a biodegradable polymer and a biostable polymer.

According to still another aspect of the present invention there is provided an anastomosis procedure, comprising: providing a medical device for implantation in a vessel as described herein; forming a plurality of vessel openings; and connecting the medical device to the plurality of vessel openings such that each vessel opening is engaged by one end of the at least one anastomotic member.

According to further features in preferred embodiments of the invention described below, the anastomosis procedure further comprises expanding the expandable supporting elements such that a pressure is generated between the non-woven cover and the plurality of vessel openings.

According to still further features in the described preferred embodiments the anastomosis procedure further comprises piercing the wall of at least one vessel using the plurality of hooks, thereby mounting the device to the at least one vessel.

According to still further features in the described preferred embodiments the piercing comprises piercing an inner wall of at least one vessel such that plurality of hooks protrudes out of an outer wall of the at least one vessel.

According to still further features in the described preferred embodiments the anastomosis procedure further comprises receiving protruding portions of the plurality of hooks using at least one perforated member mounted on the non-woven cover.

According to still further features in the described preferred embodiments the anastomosis procedure further comprises bending protruding portions of the plurality of hooks using a pressing ring.

According to still further features in the described preferred embodiments the anastomosis procedure further comprises thrusting the pressing ring using a thrust ring. According to still further features in the described preferred embodiments the thrusting is by a lever.

According to still further features in the described preferred embodiments at least one opening of the plurality of vessel openings is formed on a side of a vessel.

According to still further features in the described preferred embodiments at least one opening of the plurality of vessel openings forms a vessel end.

According to still further features in the described preferred embodiments the anastomosis procedure further comprises introducing at least one balloon into a lumen of at least one vessel, and inflating the balloon so as to reduce flow of fluids into regions being nearby to at least one opening of the plurality of vessel openings.

According to still further features in the described preferred embodiments the anastomosis procedure further comprises applying an under pressure substantially contemporaneously with the formation of the plurality of vessel openings, so as to remove fluids and tissue debris from regions being nearby to at least one opening of the plurality of vessel openings.

The present invention successfully addresses the shortcomings of the presently known configurations by providing devices, kit and methods suitable for performing anastomosis procedure. The devices, kit and methods of the present invention enjoy properties far exceeding the prior art.

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, suitable methods and materials are described below. In case of conflict, the patent

specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention is herein described, by way of example only, with reference to the accompanying drawings. With specific reference now to the drawings in detail, it is stressed that the particulars shown are by way of example and for purposes of illustrative discussion of the preferred embodiments of the present invention only, and are presented in the cause of providing what is believed to be the most useful and readily understood description of the principles and conceptual aspects of the invention. In this regard, no attempt is made to show structural details of the invention in more detail than is necessary for a fundamental understanding of the invention, the description taken with the drawings making apparent to those skilled in the art how the several forms of the invention may be embodied in practice.

In the drawings:

FIGs. 1a-b are schematic illustrations of a longitudinal cross-section (Figure 1a) and a transversal cross-section (Figure 1b) of a medical device for implantation in a vessel, according to a preferred embodiment of the present invention;

FIG. 2a is a schematic illustration of a side view of a medical device for implantation in a vessel in which an anastomotic member protrudes from its liner and cover, according to a preferred embodiment of the present invention;

FIG. 2b is a schematic illustration of the medical device of Figure 2a, after end-to-end anastomosis procedure, according to a preferred embodiment of the present invention;

FIG. 3 is a schematic illustration of a medical device for implantation in a vessel in a preferred embodiment in which the device forms a furcating structure;

FIGs. 4a-b are schematic illustrations of a longitudinal cross-section (Figure 4a) and a transversal cross-section (Figure 4b) of a medical device engaging a wall of a vessel from the side, in a preferred embodiment in which a star-shape structure is employed to anchor the medical device to the wall;

FIGs. 5a-f are schematic illustrations explaining the procedure of side-to-end implanting of a medical device a vessel, in preferred embodiments in which the device serves for end-to-side anastomosis;

FIG. 6 is a schematic illustration of a "T"-shape medical device for implantation in a vessel, in which one end can be used for end-to-side anastomosis and two other ends can be used in end-to-end anastomosis, according to a preferred embodiment of the present invention;

FIG. 7 is a is a schematic illustration of an accessory device for forming an opening in a vessel, according to a preferred embodiment of the present invention;

FIGs. 8a-b are schematic illustrations showing a technique for reducing flooding of an operation area, according to a preferred embodiment of the present invention; and

FIG. 9 is a flowchart diagram of a method of manufacturing a medical device for implantation in a vessel, according to a preferred embodiment of the present invention.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

The present invention is of a device and method which can be used in vessel implantation procedures. Specifically, the present invention can be used to replace, bypass or connect blood vessels and other fluid-transporting vessels of the body, for example, coronary arteries, peripheral blood vessels, urinary vessels and the like.

The principles and operation of a device and methods according to the present invention may be better understood with reference to the drawings and accompanying descriptions.

Before explaining at least one embodiment of the invention in detail, it is to be understood that the invention is not limited in its application to the details of construction and the arrangement of the components set forth in the following description or illustrated in the drawings. The invention is capable of other embodiments or of being practiced or carried out in various ways. Also, it is to be understood that the phraseology and terminology employed herein is for the purpose of description and should not be regarded as limiting.

Referring now to the drawings, Figures 1a-b illustrate a longitudinal cross-section (Figure 1a) and a transversal cross-section (Figure 1b) of a medical device **10** for implantation in a vessel, according to a preferred embodiment of the present invention. Device **10** is preferably tubular and comprises one or more anastomotic members **12**, a non-woven liner **14** of electrospun fibers and a non-woven cover **16** of

electrospun fibers. Anastomotic member(s) **12** preferably interpose liner **14** and cover **16**.

The electrospun fibers forming liner **14** and/or cover **16** are preferably made of a biocompatible polymer, such as, but not limited to, a biodegradable polymer, a biostable polymer or a combination thereof. For example, according to various exemplary embodiments of the present invention electrospun fibers are made of a polyurethane (*e.g.*, polyether urethane, polycarbonate urethane, siloxane-based aromatic polycarbonate urethane) found in, *e.g.*, International Patent Application Nos. WO 91/00270, WO 99/00236 and WO 98/00497). More preferably, liner **14** and/or cover **16** also comprise electrospun fibers made of a polyester (*e.g.*, polyethylene terephthalate). The advantage of using a combination of fibers made of a polyurethane with fibers made of a polyester, is that polyurethane fibers provide the liner and cover with sealing and non-thrombogenic properties, while polyester fibers provide the liner and cover with durable high tensile strength.

According to a preferred embodiment of the present invention liner **14** and/or cover **16** comprise one or more medicament incorporated therein, for a delivery of the medicament(s) into the vasculature during or after implantation. It is appreciated that the drug incorporated, as well as the concentration and method of incorporation into the device is in accordance with the type of vessel being replaced, and with the particular pathology of the patient. The preferred mechanism of medicament release from liner **14** and/or cover **16** is by diffusion, regardless of the technique employed to embed the medicament therein. The duration of medicament release in a predetermined concentration depends on several variants, which may be controlled during the manufacturing process. One variant is the chemical nature of the carrier fiber and the chemical means binding the medicament to it. This variant may be controlled by a suitable choice of the polymer(s) used in the manufacturing process. Another variant is the area of contact between the body and the medicament, which can be controlled by varying the free surface of the electrospun fibers. Also affecting the duration of medicament release is the method used to incorporate the medicament within liner **14** and/or cover **16**, as is further detailed hereinunder.

The porosity, thickness and materials of liner **14** and cover **16** are preferably selected so as to optimize the biocompatibility of device **10**. For example, the porosity, thickness and materials of liner **14** is preferably selected to prevent bleeding,

preclude preclotting and/or allow efficient endothelization. Additionally, according to various exemplary embodiments of the present invention , thickness and materials of cover **16** are selected so as to provides requisite mechanical properties, specifically high compliance and high breaking strength.

Generally, liner **14** and/or cover **16** are characterized by a porosity of at least 50 %, more preferably from about 50 % to about 85 %, a thickness of from about 50 μm to about 1000 μm, average fibers thickness of from about 100 nanometers to about 500 nanometers. Preferably, but not obligatory, the porosity and thickness of cover **16** is larger than the porosity and thickness of liner **14**.

An additional characteristic which affect the mechanical properties of device **10** is the orientation of the electrospun fibers. As further detailed hereinunder the manufacturing process of device **10** can be adapted in accordance with the desired orientation of the electrospun fibers. Preferred orientations along which the electrospun fibers are aligned include, without limitation, random alignment and circumferential alignment.

Optionally and preferably, device **10** further comprises one or more adhesive layers **15**, for adhering liner **14** to cover **16**, liner **14** to member **12** and/or member **12** to cover **16**. Adhesive layer(s) **15** can be made of any adhesive material known in the art, preferably a biocompatible adhesive material, such as, but not limited to, a thermoplastic polymer and silicon. A method of applying layer(s) **15** is provided hereinafter.

Member **12** can be a metal wire, a metal cylinder having diversified shaped orifices therein or any polymer agent having sufficient mechanical strength to mount device **10** on the vessel. Suitable members include, without limitation, members known as expandable supporting elements or stents which are found, *e.g.*, in U.S. Patent Nos. 6,019,789, 4,655,771, 5,092,877, 5,226,913, 5,741,353 and 5,849,057 the contents of which are hereby incorporated by reference. In the embodiments in which anastomotic member is a stent, member **12** can dilate a constricted blood vessel in the body vasculature. In this embodiment, member **12** is radially expandable. The expansibility of member **12** may be achieved by providing member **12** in a form of a deformable mesh of metal wires, which can be, for example, a deformable mesh of stainless steel wires. Hence, when device **10** is placed in the desired location in an artery, member **12** expands radially to substantially dilate the arterial tissues

surrounding device **10** to eradicate a flow constriction in the artery. The expansion may be performed by any method known in the art, for example by using a balloon catheter or by forming member **12** from a material exhibiting temperature-activated shape memory properties, such as Nitinol. As stated, member **12** at least partially interposes liner **12** and cover **14**. Therefore, liner **12** and/or cover **14** are preferably fabricated from non-woven elastomeric fibers, more preferably elastomeric polymer fibers, which stretch as member **12** radially expands.

According to a preferred embodiment of the present invention both liner and cover are preferably sufficiently elastic to sustain, without breakage and/or excessive resistance, the expansion of the anastomotic member which is typically from about 200 % to about 400 % in diameter. In addition, the cover preferably has high tensile strength to withstand high fluid pressure in the vessel. For example, when the device is implanted in the aorta, the cover has a tensile strength which is sufficient to withstand the aortic blood pressure without the formation of a recurrent aneurysm.

As stated, the use of polyurethane fibers in combination with polyester fibers provides sealing and non-thrombogenic properties on the one hand, and durable high tensile strength on the other hand. Such combination is preferably realized by a polyurethane matrix in which polyester fibers are distributed. The polyester fibers can be interconnected into a spatial mesh of the polyurethane fibers, or be positioned isolated in the matrix. Additionally, the polyester fibers can be either distributed uniformly within the matrix volume, or form a sparse bi-dimensional structure.

Upon expansion of the anastomotic member, the matrix experiences radial tensile forces, and, while the anastomotic member is shortened, axial compressing loads also take place. The polyester fibers and the polyurethane fibers tend to align along the force vector, resulting in a partially change of the fiber orientation. The extent of orientation on exposure to tensile loads depends on the number and density of contact points between the fibers. Due to the friction forces in the contact points, the re-orientation of the fibers is accompanied by stretching of the fibers, hence also of the entire matrix. The elongation of the fibers and matrix is directly proportional to the loading, and it prolongs until they reaches their tensile strength limit. Being less prone to tension, the polyester fibers restrain further deformation. Thus, large percentage of polyester fibers, corresponds to a lesser extent of matrix elongation and a higher tensile strength.

According to a preferred embodiment of the present invention the percentages of polyester fibers and polyurethane fibers are selected so as to optimize both elasticity (provided by the polyurethane fibers) and rigidity (polyester fibers) of the liner and cover. This can be achieved by selecting the percentages such that the elastic properties of the liner and cover match the elastic properties of the anastomotic member. In other words, the amount of polyester fibers is selected such that when the anastomotic member completes its full expansion, the polyester fiber are stretch to their maximal or close to maximal extent.

The optimal volumetric amount of polyester fiber also depends on the number of contact points among the fibers which is characterized by the porosity of the liner and cover. When the number of contact points is small, the friction forces between fibers are also small and the fibers can more freely change their orientation. Conversely, when the number of contact points is large, the re-orientation of the fibers is constrained by the friction forces, and the elongation is more pronounced. Therefore, according to a preferred embodiment of the present invention when the porosity of the liner and cover is high, larger amount of polyester fibers can be used to achieve the required rigidity. In experiments performed by the Inventors of the present invention it was found that a preferred porosity of the liner and cover is about 60-70 %, and a preferred percentage of polyester fibers is about 15-30 % by volume, where the high values (70 % porosity and 30 % polyester) corresponds to the axial orientation of polyester fibers, and the low values (60 % porosity and 15 % polyester) correspond to circumferential orientation thereof.

Referring now again to the drawings, in the embodiment shown in Figure 1a anastomotic member **12** fully superimposes liner **14** and cover **16**. However, this need not necessarily be the case, since, for some applications, it may not be necessary for anastomotic member to extend along the length of liner **14** and cover **16**.

An alternative, yet preferred, embodiment is shown in Figures 2a-b. In this embodiment, member **12** partially interposes liner **14** and cover **16**.

With reference to Figure 2a, anastomotic member **12** preferably protrudes out of cover **14** and/or liner **12**. Such protrusion facilitates the mounting of device **10** to the vessel, preferably without or with minimal sewing. Thus, according to various exemplary embodiments of the present invention, anastomotic member **12** is designed

for engaging one or more ends of device **10** to a wall of the vessel upon implantation of device **10** within the vessel.

Figure 2b is a schematic illustration of device **10** in a preferred embodiment in which end **22** of device **10** engages an inner wall **18** of a vessel **20**. As shown in Figure 2b, anastomotic member **12** is in contact with inner wall **18** thus fixing device **10** in its proper place, while cover **16** is flush with an outer wall **30** of vessel **20**. Thus, the present embodiment successfully enables the attachment of device **10** with vessel **20** while ensuring a smooth joining between device **10** and vessel **20**. Preferably, a pressing ring **24** is mounted on outer wall **30** such that the wall of vessel **20** is subjected to pressure both from its inner side **18** (via forces applied by member **12**) and its outer side **30** (via forces applied by ring **24**). Ring **24** can be made of an elastic biocompatible material (*e.g.*, an elastic polymer), a metal, a mesh of wires or any other structure which is capable of applying an inward, radial-oriented, force.

Many shapes of device **10** are contemplated, depending on the medical procedure in which device **10** is used. Preferably, the shape of device **10** is selected in accordance with the type of vessel (*e.g.*, aorta, carotid, coronary artery, *etc.*) and the type of anastomosis required (*e.g.*, end-to-side anastomosis, end-to-end anastomosis).

Reference is now made to Figure 3 which is a schematic illustration of a portion device **10** in a preferred embodiment in which device **10** forms a furcating structure **26** having a plurality of tubular branches **28**. In the exemplifying embodiment shown in Figure 3a, device **10** forms a "Y"-shape, *i.e.*, a bifurcating structure with three ends. But this need not necessarily be the case since, for some applications, it may be desired to have other shapes of bifurcating structure (*e.g.*, a "T"-shape) or other furcating structures (*e.g.*, trifurcating structures). Additionally, each branch of device **10** can be shaped differently so as to allow the use of different branches for different types of anastomoses or different vessels.

Reference is now made to Figures 4a-b which are schematic illustrations of device **10** in a preferred embodiment in which device **10** serves for end-to-side anastomosis. These embodiments can be used, for example, when device **10** is used during a heart bypass procedure in which case device **10** channels the blood flow around the blocked portions of the coronary arteries. Thus, one end of device **10** can be connected to the side of the aorta and the other end(s) can be connected to the side or end of one or more diseased coronary arteries. According to the presently preferred

embodiment of the invention member **12** is expandable and comprises a plurality of hooks **32**, which may form, for example, a star-shape structure **33**. In use, once end **50** of device **10** is positioned in an opening in the wall of vessel **20**, member **12** and star-shape structure **33** preferably expand, such that member **12** is pressed against the wall of vessel **20** and star-shape structure **33** anchors device **10** in its position. In various exemplary embodiments of the present invention, an additional circular member **31** (which may be, for example, similar to pressing ring **24**) is mounted on cover **16** so as to prevent device **10** from moving inward into the lumen of vessel **20**.

Reference is now made to Figures 5a-f which are schematic illustrations explaining the procedure of side-to-end implantation of device **10**, according to various exemplary embodiments of the present invention.

Referring to Figure 5a, according to various exemplary embodiments of the present invention member **12** is manufactured as a rhomboidal mesh of wires (*e.g.*, a stent), capable of expanding radially and equipped with hooks **32**. The number of hooks preferably depends on the diameter of member **12**. Typically, from 2 to 10 hooks, more preferably from 6 to 12 hooks are used. Hooked **32** is preferably fixed to the upper nodular parts of the rhomboids such that when member **12** expands to a direction designated by double headed arrow **34**, hooks **32** move to the direction designated by arrow **36**.

Figure 5b illustrates device **10** in a pre-implantation state, *i.e.*, prior to its connection to the vessel wall. In this state, member **12** is still in its reduced diameter and the level of hooks **32** slightly exceeds cover **16**. The height of hooks **32** above cover **16** (designated δ in Figure 5b) is preferably from about 1 mm to about 6 mm.

As used herein the term "about" refers to $\pm$ 10 %.

Figure 5c illustrates the implantation of device **10** within vessel **20**. An opening **38** is made in the wall of vessel **20** such that its diameter insignificantly exceeds outer diameter of device **10** in its pre-implantation state. Device **10** is introduced into opening **38** and member **12** expands (*e.g.*, using a catheter balloon). As member **12** expands, cover **16** come into tense contact with the wall of opening **38** thus sealing it. At the same time, hooks **32** move towards vessel **20** pierce its inner wall **21** and protrude out of its outer wall **23**. The displacement of hooks **32** can be further enhanced by pulling device **10** outside opening **38** once member **12** is in its expanded state.

As will be appreciated by one of ordinary skill in the art, in its final position, device **10** cannot come out of the opening, as it is held by hooks **32**. Additionally, device **10** is prevented from falling into the vessel by the pressure fluids (*e.g.*, blood) flowing through the vessel, and by a friction force between the wall of the vessel and cover **16** which is enhanced by the pressure applied by member **12**. The connection reliability can be further increased by bending the protrusion of hooks **32** or by employing more hooks or other elements, *e.g.*, discs, rings and the like.

Figure 5d illustrates one preferred embodiment in which a perforated member **40** (*e.g.*, a disc) is utilized for fixing device **10** to vessel **20**. Hence, according to the presently preferred embodiment of the invention, protrusions **33** of hooks **32** can be passed through holes in member **40**, so as to prevent detachment of hooks **32** from vessel **20**. Member **40** can be made, for example, of metal or polymer mesh.

Figure 5e illustrate an additional embodiment in which a thrust ring **42** and/or a pressing ring **44** are utilized for fixing device **10** to vessel **20**. Thrust ring **42** is preferably fixed to cover **16** (*e.g.*, using a balloon), and pressing ring **44** is positioned closed to the protruding portions **33** of hooks **32**. Pressing ring **44** is preferably equipped with a groove **46** shaped so as to grasp and bend protruding portions **33**, as a predetermined angle (say, bending of about 40-70 degrees). Preferably, a triangle-sectioned groove is employed. A contact between pressing ring **44** and thrust ring **42** can then be established, for example, using a pair of levers **46** which move **44** in the direction of **42**.

Figure 5f illustrates another preferred embodiment in which device **10** comprises a ring-shaped protuberance **48**. Protuberance **48** can be integrated with or attached to cover **16**. Upon expansion of member **12**, hooks **32** pierce the wall of vessel **20**, and protuberance **48** prevents, at least partially, the displacement of device **10** inside opening **38**.

As stated, device **10** can form a furcating structure, whereby different branches of device **10** can be used for different anastomoses or different vessels. One such embodiment is shown in Figure 6.

Figure 6 schematically illustrate a preferred embodiment of the present invention in which device **10** forms a "T"-shape, having a first end **50** a second end **52** and a third end **54**. In the exemplified embodiment shown in Figure 6, end **50** serves for end-to-side anastomosis and ends **52** and **54** serve for end-to-end connection. This

embodiment is particularly useful for heart bypass procedure, whereby end **50** is connected to the aortal wall, *e.g.*, using hooks **32** as further detailed hereinabove, and ends **52** and **54** are connected to ends of the diseased coronary arteries.

One of the difficulties for a surgeon performing a bypass operation, or any other operation in which the aorta is opened while the heart is beating, is the high aortic blood pressure. Upon the formation of the opening of the aortal wall, blood starts to flow through the opening resulting in sever blood loss. The present embodiments successfully provide an accessory device **60** for forming an opening in a vessel, while substantially reducing or preventing the flooding of the operation area by blood.

Reference is now made to Figure 7 which is a schematic illustration of accessory device **60**, according to a preferred embodiment of the present invention. One or more units of device **60** can be presented, if desired, together with one or more units of device **10**, in a pack or dispenser device, such as an FDA approved kit. The pack may be accompanied by instructions for use. The pack may also be accommodated by a notice in a form prescribed by a governmental agency.

Hence, device **60** preferably comprises a tubular encapsulation **62** for encapsulating device **10**, preferably in a manner such that device **10** is movable along a longitudinal axis **64** of encapsulation **62**. Encapsulation **62** is preferably made of metal (*e.g.*, stainless steel) or any other material (*e.g.*, a polymer) having a sufficient strength to withstand aortic blood pressure. According to various exemplary embodiments of the present invention device **60** further comprises a generally circular cutting member **66** integrated with or attached to encapsulation **62**. Additionally device **60** comprises a vacuum channel **68**, preferably formed on the side of tubular encapsulation **62**.

In use, member **12** is preferably expanded (*e.g.*, using a balloon), until cover **16** is pressed to the inner wall of encapsulation **62** to form a hermetically sealed connection therebetween. Subsequently, cutting member **66** is brought into contact with the vessel wall (not shown) to form an opening therein. Cutting member **66** can form the opening in the vessel wall using any technique known in the art, such as, but not limited to, cutting and burning. At the same time, or shortly thereafter, an under pressure is formed in vacuum channel **68**, *e.g.*, using a pump (not shown), so as to

channel an efflux of biological material (tissue debris, blood) from encapsulation **62**, thereby to clear the operation area.

Once the opening is formed, the diameter of member **12**, hence also of cover **16**, can be reduced (*e.g.*, by deflating the balloon), and device **10** can be advanced within encapsulation **62** so as to engage the opening.

Figures 8a-b illustrate an alternative embodiment for reducing flooding of the operation area, where Figure 8b is a cross-sectional view along the cut designated **A-A** in Figure 8a. In this embodiment, a balloon **70** is inserted to the lumen of the vessel. For example, when the vessel is a blood vessel, balloon **70** can be inserted from a far location using a catheter inserted, *e.g.*, through an incision in the skin of the groin and the wall of the femoral artery. Balloon **70** is preferably shaped so as to prevent fluid communication between operation area **72** and an unblocked portion **71** of the lumen. More specifically, upon the inflation of balloon **70**, fluids (*e.g.*, blood) continue to flow through portion **71** of the lumen, substantially without flooding operation area **72**, which is at least partially isolated therefrom.

According to another aspect of the present invention there is provided a method of manufacturing a medical device for implantation in a vessel. The method can be used, for example, for manufacturing medical device **10**.

Reference is now made to Figure 9 which is a flowchart diagram of the method, according to various exemplary embodiments of the present invention. It is to be understood that, unless otherwise defined, the method steps described hereinbelow can be executed either contemporaneously or sequentially in many combinations or orders of execution. Specifically, the ordering of the flowchart of Figure 9 is not to be considered as limiting. For example, two or more method steps, appearing in the following description or in the flowchart of Figure 9 in a particular order, can be executed in a different order (*e.g.*, a reverse order) or substantially contemporaneously. Additionally, selected method steps, appearing, for the sake of brevity only once in Figure 9, can be can be executed a plurality of times (*e.g.*, twice).

Referring to Figure 9, the method begins at step **80** and preferably proceeds to step **82** in which one or more anastomotic members are provided. Preferably, one or more units of anastomotic member **12** are provided. The method continues to step **84** which represents an electrospinning process in which a first liquefied polymer is dispensed on a precipitation electrode so as to provide a non-woven liner, such as liner

14. The diameter of the precipitation electrode is preferably from about 10 mm to about 30 mm.

According to a preferred embodiment of the present invention the precipitation electrode is shaped in accordance with the desired shape of the device. For example, for a tubular device (see, *e.g.*, Figures 1a-2b) a tubular precipitation electrode is used; for a furcating device, a furcating (*e.g.*, bifurcating, trifurcating) precipitation electrode is used. In any event, the electrospinning process is executed such that all sides of the precipitation electrode are covered by electrospun fiber. As will be appreciated by one ordinarily skilled in the art, this can be done by rotation the precipitation electrode or the mechanism from which the liquefied is dispensed. The rotation can be done continuously while the liquefied polymer is dispensed, or in a discrete manner such that the electrospinning is repeated a plurality of times, each time for different orientation of the precipitation electrode.

When the precipitation electrode is tubular, it is sufficient to rotate the electrode about its longitudinal axis. When a furcating precipitation electrode is used, several axes of rotation are preferably employed. For example, a longitudinal axis and an axis perpendicular to the longitudinal axis can be used. The method preferably proceeds to step **86** in which the anastomotic member(s) are mounted onto the precipitation electrode, such that at least a portion of each anastomotic member superimposes at least a portion of the liner, as further detailed hereinabove (see, *e.g.*, Figure 1a for the embodiment in which the anastomotic member is flush with the liner and Figure 2a for the embodiment in which the anastomotic member protrudes out of the liner).

The method preferably continues to step **88** which represents an additional electrospinning process in which a second liquefied polymer is dispensed so as to form non-woven cover of electrospun fibers. The cover preferably has the characteristics of cover **16** as further detailed hereinabove. The second liquefied polymer can be dispensed on the precipitation electrode, the liner and/or the anastomotic member(s), depending on the level of superimposing between the cover, the liner and the and anastomotic member(s). Optionally and preferably, step **88** is accompanied by a formation of a ring-shaped protuberance (*e.g.*, protuberance **48**, see Figure 5f) onto the cover. This can be done by increasing the amount of fibers precipitation in a predetermined location, so as to thicken the cover thereby to form the protuberance.

The method preferably comprises a step **94** in which a pressure is applied so as to achieve higher level of adherence between the liner, cover and anastomotic member. Step **94** can be executed more than once. Preferably, but not obligatory, step **92** is executed a first time subsequently to step **84** and a second time subsequently to step **86**.

The electrospinning steps may be performed using any electrospinning apparatus known in the art. According to the electrospinning method, the liquefied polymer is charged and drawn into a dispensing electrode, and then, subjected to an electric field, dispensed in a direction of the precipitation electrode. Moving with high velocity in the inter-electrode space, jets of liquefied polymer evaporate, thus forming fibers which are collected on the surface of the precipitation electrode. A typical thickness of the fibers thus formed ranges between 100 nanometers to about 500 nanometers.

It was found by the Inventor of the present invention that randomized structure surface comprising 100-200 nm fibers possesses non-thrombogenic properties. Devices with such inner surface are capable of efficient endothelization and have good general coalescence. Additionally it was found by the Inventor of the present invention that a liner and/or the cover thickness of less than 400-500 μm with about 90 % of the fibers having thickness of about 1-2 μm, have good sealing properties and prevents blood leakage.

The orientation of the fibers can be controlled by varying the direction of the electric field (*e.g.*, using more than one electrode). As stated, such predetermined orientation affects the mechanical characteristics of the device.

The advantage of using the electrospinning method for fabricating the medical device is flexibility of choosing the polymer types and fibers thickness, thereby providing a final product having the required combination of strength, elastic and other properties as delineated herein. In addition, the electrospinning method has the advantage of allowing the incorporation of various chemical components, such as medicaments, to be incorporated in the fibers, *e.g.*, by dissolving or dispersing such medicaments in the liquefied polymers prior to electrospinning.

Thus, according to a preferred embodiment of the present invention, the method may further comprises an optional step **90** in which one or more medicaments are incorporated within the liquefied polymers. Step **90** can be executed more than

once. Preferably, but not obligatory, step **90** is executed a first time in combination (*e.g.*, prior, subsequently or contemporaneously) with step **84** and a second time in combination with step **86**. The medicament(s) may be of any type which can be useful in treating the lumen of the vessel. For example, when the vessel is a blood vessel, anti-platelets and anticoagulants can be incorporated to control platelet aggregation and adhesion; and growth factor, receptor blockers and antagonists may be used to limit the normal repair response. Preferably, but not obligatory, the medicament is loaded into biodegradable polymer fibers, which are preferably axially oriented hence do not essentially contribute to the radial strength. Such incorporation of medicaments results in slow release of drugs upon biodegradation of the fibers. The medicament can also be in a powder form or micro-encapsulated particulates form so that it can be sprayed as a shower of particles onto a liner **14** and/or cover **16**, depending on the scheduling of step **90**. Representative examples of medicaments which can be incorporated in the liner and/or cover include, without limitation, heparin, tridodecylmethylammonium-heparin, epothilone A, epothilone B, rotomycine, ticlopidine, dexamethasone, caumadin, and other pharmaceuticals falling generally into the categories of antithrombotic drugs, estrogens, corticosteroids, cytostatics, anti-coagulant drugs, vasodilators, and antiplatelet drugs, trombolytics, antimicrobials or antibiotics, antimitotics, antiproliferatives, antisecretory agents, nonsterodial antiflammentory drugs, grow factor antagonists, free radical scavengers, antioxidants, radiopaque agents, immunosuppressive agents and radio-labeled agents.

One or more of the electrospinning steps (steps **84** and **88**) preferably comprises the use of two different polymers. For example, according to various exemplary embodiments of the present invention the liner and/or cover are made of polyurethane fibers as well as polyester fibers, so as to achieve the aforementioned properties of elasticity and rigidity. According to a preferred embodiment of the present invention the same or similar solvents are used for liquefying the polyurethane and polyester. The advantage of this embodiment is that the use of similar or identical solvents facilitates the bonding between the polyurethane fibers and the polyester fibers. Preferred solvents for liquefying the polymers include, without limitation, solvents which are based on phenol, methylene chloride and trifluoroacetic acid. While reducing the preset invention to practice it was uncovered that the bonding strength between the polyurethane matrix and polyester fiber is significantly increased

when a small amount of polyurethane (*e.g.*, from about 10 % to about 20 %) is added to polyester solution.

According to a preferred embodiment of the present invention the method comprises an additional step **92** in which one or more adhesive layers are formed on the liner, the anastomotic member and/or the liner. Step **92** can be executed more than once. Preferably, but not obligatory, step **92** is executed a first time subsequently to step **84** and a second time subsequently to step **86**. The formation of adhesive layer can be effected from several procedures in any combination.

Hence, in one such procedure, the final stage of liner generation and the initial stage of cover generation are preferably conducted in an elevated productivity, typically from about 1.5-fold productivity to about 3-fold productivity. Elevated productivity can be achieved, for example, by providing higher pressure or higher amount of liquefied polymer in the electrospinning process. This procedure can also include the replacement of the liquefied polymers (the polymer types and/or the solution in which they are dissolved). It was found by the Inventor of the present invention that the use of liquefied polymer with higher boiling point in the final stage of liner generation provides good adhesive properties which are preserved during the mounting of the anastomotic member. Similarly, the use of liquefied polymer with higher boiling point in the final stage of liner generation provides good adhesive properties between the anastomotic member and the cover.

In another such procedure, an intermediate adhesion layer is preferably electrospun prior to- and/or immediately after the execution of step **86**. The intermediate adhesion layer is preferably made of a thermoplastic polymer having a characteristic melting temperature which is considerably lower than the characteristic temperature of the first and second polymers used for the liner and cover. The present procedure is preferably supplemented by step **96** in which, once the electrospinning processes are completed, the device is heated to a temperature which is above the characteristic melting temperature of the intermediate adhesion layer but below the characteristic melting temperature of the liner and the cover. The heating results in a conversion of the intermediate adhesion layer to a viscous-flowing state and promotes the adhesion of the anastomotic member to the liner and cover.

For example, the liner and cover can be made of polycarbonate urethane with melting point of about 230 °C, and the intermediate adhesion layer can be made of

polycarbonate urethane with melting point of about 160 °C. In this example, the device can be heating to a temperature of about 160-170 °C, resulting in the desired adherence effect.

An additional procedure suitable for achieving adherence between the liner and cover and the anastomotic member, is represented by step **98**, which is preferably executed prior to the mounting of the anastomotic member on the precipitation electrode. In step **98**, the anastomotic member is preferably dipped into an adhesive solution, such as, but not limited to, a silicon rubber solution. The dipping is preferably supplemented by a thermal treatment of the anastomotic member so as to allow chemical cross-linking between the anastomotic member and the adhesive solution. For the case of silicon rubber solution, the heating can be to a temperature of 100-110 °C for about 30 minutes.

In a further step **100** of the method, one or more perforated members are mounted onto the cover. The perforated member(s) are preferably several units of perforated members **40** as further detailed hereinabove. The method can also comprise (in addition or as an alternative to step **100**) a step **102** in which a pressing ring (*e.g.*, pressing ring **44**) and, optionally a thrust ring (*e.g.*, thrust ring **42**) and a lever (*e.g.*, lever **46**) can be mounted on the cover, preferably according to the construction shown in Figure 5e and further detailed hereinabove.

Following is a non exhausted list of biostable polymers which can be used in the liner and/or cover. Polycarbonate based aliphatic polyurethanes, siloxane based aromatic polyurethanes, polydimethylsiloxane and other silicone rubbers, polyester, polyolefins, polymethyl- methacrylate, vinyl halide polymer and copolymers, polyvinyl aromatics, polyvinyl esters, polyamides, polyimides, polyethers and many others that can be dissolved in appropriate solvents and electrically spun on the stent.

Biodegradable fiber-forming polymers that can be used include, without limitation poly (L-lactic acid), poly (lactide-co-glycolide), polycaprolactone, polyphosphate ester, poly (hydroxy- butyrate), poly (glycolic acid), poly (DL-lactic acid), poly (amino acid), cyanocrylate, some copolymers and biomolecules such as DNA, silk, chitozan, collagen and cellulose.

These hydrophilic and hydrophobic polymers which are readily degraded by microorganisms and enzymes are suitable for encapsulating material for medicaments. In particular, polycaprolacton has a slower degradation rate than most other polymers

and is therefore especially suitable for controlled-release of pharmaceutical agent over long periods of time scale ranging from about 2 years to about 3 years.

It is appreciated that certain features of the invention, which are, for clarity, described in the context of separate embodiments, may also be provided in combination in a single embodiment. Conversely, various features of the invention, which are, for brevity, described in the context of a single embodiment, may also be provided separately or in any suitable subcombination.

Although the invention has been described in conjunction with specific embodiments thereof, it is evident that many alternatives, modifications and variations will be apparent to those skilled in the art. Accordingly, it is intended to embrace all such alternatives, modifications and variations that fall within the spirit and broad scope of the appended claims. All publications, patents and patent applications mentioned in this specification are herein incorporated in their entirety by reference into the specification, to the same extent as if each individual publication, patent or patent application was specifically and individually indicated to be incorporated herein by reference. In addition, citation or identification of any reference in this application shall not be construed as an admission that such reference is available as prior art to the present invention.